REMARKS

In the present communication, no claims have been amended, added, or cancelled. The Examiner withdrew Claims 15-16, 18-20, 22, and 28 from consideration. As such, Claims 14, 17, 21, and 23-27 are currently pending and under Examination.

I. Obviousness Rejection

The Examiner issued a single rejection, rejecting Claims 14, 17, 21, and 23-27 under 35 U.S.C. 103(a) as allegedly unpatentable over Koduri et al. in view of Urbanie et al., Wagner et al., Song et al., and Pira et al. Applicants respectfully disagree with this rejection.

As part of this rejection, in addressing independent Claim 14, the Examiner cites Koduri et al. as teaching administration of IVIG to an HIV infected patient, and Pira et al. as teaching monitoring T-cell diversity in an HIV infected patient. In particular, the Examiner states:

> [I]t would have been obvious to one of ordinary skill in the art to monitor T cell diversity in view of the teaching of Pira et al. (see entire document). In particular, Pira et al. taught that in order to monitor the cellular immune state of a HIV patient, CD4 T cells should be monitored by defining the specificity or clonal diversity (see Abstract). Upon reading the prior art, one of ordinary skill in the art would have been reasonably expected to monitor T cell diversity in subject with HIV infection. (Office Action, page 5).

Applicants respectfully submit that BOTH Koduri et al. and Pira et al. suggest that it is not useful to measure T cell diversity in HIV patients, and that one of skill in the art would have no reason to combine the references (e.g., based on the lack of motivation in Koduri et al.).

A. Koduri et al.

Koduri et al. use IVIG to treat parvovirus infection in HIV patients. The authors' rationale was based on the assumption that since parvovirus infection is prevalent in the population, IVIG contains antibodies of therapeutic value against parvovirus. In fact, the authors stated:

> The IgG antibodies to B19 were intermittently positive in some patients during follow up, and this was attributed to the passive acquisition of the antibody through Ig infusion.

Thus, since the authors expected a <u>direct</u> anti-viral effect provided by antibodies administered passively, the therapeutic effect <u>is independent of properties of T cells.</u> As such, one of ordinary

skill in the art of administering IVIG to treat parvovirus infection in HIV patients would not have been motivated to monitor T cell diversity as this is not relevant to IVIG treatment according to Koduri et al.

B. Pira et al.

Pira et al. found that in spite of decreased proliferative responses to *P. carinii* and Cytomegalovirus, T cells obtained from HIV infected subjects generated pathogen-specific T cell clones that had "normal" V beta family usage and sequences with "normal" CDR 3 length distributions. The authors concluded that "a reduced CD4 response is not necessarily due to loss of one or more specific clonal responses, but rather that each clone has lost a fraction, but not all of its cells." This conclusion implies that analysis of clonal diversity as preformed by the authors does not explain HIV-associated T cell immunodeficiency and therefore one of ordinary skill would decide against monitoring T cell diversity in subjects with HIV.

C. No Reason to Combine References

In light of the teachings in Koduri et al. and Pira et al. outlined above, Applicants respectfully submit that no reason has been established to combine these references. The mere fact that both patient populations are HIV patients is not enough. In particular, the primary reference, Kodori et al., shows clearly that one of skill giving IVIG to an HIV patient would *specifically not have a reason* to then measure T cell diversity given that it's therapeutic effect is independent of T cell diversity. Furthermore, Pira et al. indicate that the T cell monitoring would not be useful for HIV patients. In light of the teachings in these references, any attempt to combine these two references is, therefore, necessarily relying on hindsight reconstruction using the present application as a guide to assemble the elements. As such hindsight reconstruction is not permissible, Applicants respectfully submit that this rejection should be withdrawn and the claims allowed.

CONCLUSION

Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourage the Examiner to call the undersigned at 608-662-1277.

Dated: May 24, 2011

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